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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/647,071	SWAIN ET AL.	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 11, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *125,126,128,131-138 and 142* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *125,126,128,131-138 and 142* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/26/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 11, 2009 has been entered.

Status of the Claims

2. Claims 1-99, 105-108, and 110 were canceled, claims 101-103 and 109 were amended, and new claims 111-124 were added in the amendment to the claims received on June 1, 2006.

The amendment to the claims received on February 16, 2007 amended claims 100-101, 118; canceled claims 102, 114-116; and added new claims 125-140.

The amendment to the claims received on October 9, 2007 canceled claims 100-101, 103-104, 109, 111-113, 117-124, 127, and 130 and amended claims 125 and 129.

The amendment to the claims received on June 12, 2008 amended claim 125, canceled claims 129 and 139-140, and added new claims 141-142.

The amendment to the claims received on January 26, 2009 amended claims 125-126, 128, 131-138, and 142 and canceled claim 141.

The amendment to the claims received on June 11, 2009 amended claims 125 and 142. Please note: claim 132 has an improper status identifier of "presently amended" (see claim objection below).

Claims 125-126, 128, 131-138, and 142 are currently pending and under consideration.

Election/Restrictions

3. Applicants elected, with traverse, Group I (previous claims 100-104) in the reply filed on June 1, 2006. The traversal was on the ground(s) that a serious burden to search Groups I and III did not exist. The traversal was found persuasive. Therefore, the restriction between Groups I and III (i.e. previous claim 109) was withdrawn. However, applicants did not traverse the restriction between Group I and Groups II or IV. The restriction was made final in the Office action mailed on August 17, 2006.

Priority

4. The present application claims status as a CON of 10/115,580 filed April 1, 2002 which is a CON of 09/882,803 filed June 14, 2001 which is a CON of 09/257,821 filed February 25, 1999 which is a CON of 08/720,487 filed September 30, 1996 (now U.S. Patent 5,876,727) which is a CIP of 08/563,673 filed November 28, 1995 (now U.S. Patent 5,760,184) which is a CIP of 08/414,971 filed March 31, 1995.

5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/414,971, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 08/414,971 does not disclose nicotine or nicotine derivatives (i.e. nicotine metabolites of present Figure 19, nicotine-1'-N-oxide, trans-3'-hydroxycotinine, or nicotine glucuronide). In addition, application No. 08/414,971 does not disclose branch CJ 11.

The disclosure of the prior-filed application, Application No. 08/563,673, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 08/563,673 (U.S. Patent 5,760,184 does not disclose nicotine derivatives (i.e. nicotine metabolites of present Figure 19, nicotine-1'-N-oxide, trans-3'-hydroxycotinine, or nicotine glucuronide).

Therefore, the priority date for the present claim limitations of nicotine derivatives and CJ 11 is September 30, 1996 (i.e. filing date of U.S. application 08/720,487 which is now U.S. Patent 5,876,727). The priority date for the claim limitation of nicotine is November 28, 1995 (i.e. filing date of U.S. application 08/563,673 which is now U.S. Patent 5,760,184). Therefore, the priority for the presently claimed invention as a whole is September 30, 1996.

Arguments and Response

6. Applicants contend that 08/563,673 disclose nicotine derivatives. However, nicotine derivatives including the ones in the present specification (i.e. nicotine metabolites of present Figure 19, nicotine-1'-N-oxide, trans-3'-hydroxycotinine, or nicotine glucuronide) are not

present in 08/563,673. While the genus of drug derivative and the subgenus of cocaine derivative are present in the disclosure of 08/563,673, nicotine derivative is not disclosed. Therefore, the priority date for the presently claimed invention is September 30, 1996.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on January 26, 2009 is being considered by the examiner in part (see below).

8. The information disclosure statement filed January 26, 2009 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered (i.e. references 88-89 were not provided). Applicants are respectfully requested to provide a new IDS along with the copies of references 88-89.

Invention as Claimed

9. A pharmaceutical composition comprising a hapten-carrier conjugate said pharmaceutical composition comprising at least one hapten which is nicotine or a nicotine derivative and at least one carrier which is a pseudomonas exotoxin and wherein the hapten and the carrier are linked by a branch selected from the group of chemical moieties CJ 0, 1, 1.1, 2, 2.1, 2.2, 2.3, 3, 3.1, 4, 4.1, 5, 5.1, 6, 7, 7.1, 8, 8.1, 9, 10, 11, and 11.1 and variations thereof.

New Objection

Claim Objections

10. Claim 132 is objected to because of the following informalities: the claim has a status identifier of "Presently Amended" while the status identifier should be "Previously Presented". Appropriate correction is required.

Withdrawn Rejections

11. The declaration under 37 CFR 1.132 filed June 11, 2009 is sufficient to overcome the rejection of claims 125-126, 128, 131-138, and 142 based upon 35 U.S.C. 102(e) as being anticipated by Swain et al. U.S. Patent 6,054,127 (effective filing date of March 31, 1995).

12. The rejection of claims 125-126, 128, 131-138, and 142 under 35 U.S.C. 103(a) as being unpatentable over Walling et al. U.S. Patent 5,164,504 issued November 17, 1992 and Green et al. U.S. Patent 5,601,831 issued February 11, 1997 are withdrawn in view of the claim amendments received on June 11, 2009 (i.e. elicits nicotine-specific antibodies in a human).

Maintained Rejections

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 125-126, 128, 131-138, and 142 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection. Applicants point to page 10, lines 26-35; page 11, lines 4-8; page 24, lines 19-23; page 114, line 33 to page 125, line 1; and page 119, lines 4-12 to support the claim amendments received on January 26, 2009. However, the previously mentioned sections of the specification do not provide support for the Markush group for Q (e.g. Q is H, OH, etc.; see independent claim 125). Therefore, the Markush group is considered new matter.

Arguments and Response

15. Applicants' arguments directed to the rejection under 35 USC 112, first paragraph (new matter), for claims 125-126, 128, 131-138, and 142 were considered but are not persuasive for the following reasons.

Applicants contend that support can be found at page 114, line 33 to page 115, line 1 and page 119, lines 4-12.

Applicants' arguments are not convincing since the present specification only contains 113 pages.

New Rejections

Claim Rejections - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 125-126, 128, 131-138, and 142 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection. The specification does not provide support for a pharmaceutical composition comprising a hapten which is nicotine or a nicotine derivative, a carrier which is pseudomonas exotoxin, and linkers represented by the various formulas of the CJ reference numbers "which elicits nicotine-specific antibodies in a human".

18. Claims 125-126, 128, 131-138, and 142 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **written description** rejection.

With regard to the written description requirement, the attention of the Applicant is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)] (the case is referred to herein as "*Lilly*").

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

Although directed to DNA compounds, this *Eli Lilly* holding would be deemed to be applicable to any compound or a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). In this regard, applicant is further referred to *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); and *Univ. Of Rochester v G. D. Searle and Co.* 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) publication pending.

Additionally, *Lilly* sets forth a two part test for written description:

A description of a genus of cDNA's may be achieved by means of a recitation of: a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus OR of a recitation of structural features common to the members of the genus. See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]hc description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Additionally, Cf. University of Rochester v G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc., No. 03-1304, 2004 WL 260813 (Fed. Cir., Feb. 13, 2004) held that:

> *Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.*

In the present instance, the specification discloses only limited examples that are not representative of the claimed genus of a "pharmaceutical composition comprising nicotine or a nicotine derivative which elicits nicotine-specific antibodies in a human"; nor do the claims recite sufficient structural feature(s) which is(are) common to members of the genus sufficient to demonstrate possession of the genus. The instant claims refer to nicotine and nicotine derivatives as the haptens, pseudomonas exotoxin as the carrier, and linkers of various formula. The claimed "pharmaceutical composition" is defined by functional properties (e.g. "elicits a nicotine-speicifc antibodies in a human") without providing the structure necessary to elicit a

specific antibody response to nicotine in a human (i.e. minimum structure required for a specific antibody response against nicotine in a human). Will any nicotine derivative linked to pseudomonas exotoxin "elicit nicotine-specific antibodies in a human"? The CAFC held that a functional definition is insufficient to adequately describe a product, therefore, an adequate written description not based on a functional definition is necessary.

The Examiner further notes the present claims stated by Applicant are broader in scope that those that were held to be impermissible in *Lilly* because, unlike *Lilly*, Applicants' claims encompass a vast number of "nicotine derivatives" (i.e. derivative is not further defined by the present specification). The scope of these claims include a vast number of structures because the specification and claims do not place any limit on the number of components (e.g. molecules, R groups, etc.) or the type of components (e.g. chemical, peptide, etc.) to make a "nicotine derivative". Furthermore, the specification and claims do not place any limit on the number of components, the types of components, or the manner in which the components might be connected to form a pharmaceutical composition comprising a nicotine derivative that elicits an antibody response specifically to nicotine in humans. Therefore, Applicant is using an inadequately described "nicotine derivative" to inadequately describe the claimed "pharmaceutical composition". In addition, the "elicits nicotine-specific antibodies in a human" claim language further exacerbates this problem because the conditions under which a nicotine derivative will elicit a nicotine-specific antibody response in a human are not specified. Consequently, there is no teaching that would allow a person of skill in the art to determine *a priori* that the Applicant was in possession of the full scope of the claimed invention at the time of filing because there is no common structural attributes that can link together all of the claimed

"nicotine derivatives" or the "pharmaceutical composition" that will "elicit nicotine-specific antibodies in a human".

The general knowledge and level of skill in the art for the relationship between antigens and antibodies and utilization of adjuvants and carriers to enhance the immune response is high, the general knowledge and level of skill in the art for producing pharmaceutical compositions that are efficacious and safe in humans is lower (i.e. few drugs reach phase IV clinical trials; references will be provided if requested by applicants). Therefore, the knowledge and level of skill does not supplement the omitted description because specific, not general, guidance is needed for the "pharmaceutical composition which elicits nicotine-specific antibodies in humans". Since the disclosure fails to describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof, and because the genus is vast and highly variant (e.g. nicotine derivative is not defined by the present specification), the limited examples in the specification (e.g. four nicotine metabolites in Figure 19; no examples of nicotine derivatives producing nicotine-specific antibodies in humans in the present specification) is insufficient to teach the entire genus.

The specification discloses only limited examples that are not representative of the claimed genus of a "nicotine derivative"; nor do the claims recite sufficient structural feature(s) which is(are) common to members of the genus sufficient to demonstrate possession of the genus. Therefore, the teachings in the specification are general teachings relating without guidance as to the individual components of the product. In addition, there are numerous "nicotine derivatives" that could be employed in the invention with little direction or guidance for one of skill in the art to practice the claimed invention (i.e. structure necessary to produce

nicotine-specific antibodies in humans). The expedient statements in the specification do not relate to an adequate disclosure or how to make and use the claimed invention. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to adequately describe the vast genus. Thus, Applicant does not appear to be in possession of the claimed genus.

19. Claims 125-126, 128, 131-138, and 142 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a "hapten-carrier conjugate", the specification does not reasonably provide enablement for "a pharmaceutical composition which elicits nicotine-specific antibodies in a human". The specification does not enable a person skilled in the art to make and use the invention commensurate in scope with the claim. This is a **scope of enablement** rejection.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The level of skill in the art;
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;

8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure.

See *In re Wands* USPQ 2d 1400 (CAFC 1988):

The breadth of the claims and the nature of the invention:

Although requiring a specific carrier (i.e. pseudomonas exotoxin) and specific linkers (i.e. CJ 0 to CJ 11), the claims also refer to nicotine or nicotine derivatives wherein "nicotine derivatives" are not specifically defined in either the claims or the specification. Accordingly, the claims encompass a vast number of "nicotine derivatives". Intended use as a "pharmaceutical composition" which "elicits nicotine-specific antibodies in humans" does not provide any information regarding the required structure of the "nicotine derivatives" (e.g. required core structure, etc.). Accordingly, the claim scope is unduly broad with respect to the encompassed nicotine derivatives.

The state of the prior art and the level of predictability in the art:

Pharmaceutical compositions comprising nicotine or nicotine derivatives conjugated to pseudomonas exotoxin that elicit nicotine-specific antibodies in humans is highly unpredictable in the art, particularly regarding eliciting nicotine-specific antibodies in humans. Various issues may arise during pre-clinical or early clinical experimentation related to toxicity, efficacy, specificity for intended targets (i.e. nicotine), unacceptable side effects (e.g. risk/benefit analysis), delivery formulation (e.g. oral, intravenous, etc.), pharmacokinetics, pharmacodynamics, development of drug resistance, monotherapy verses combination therapy, etc. While there is a need in the art for successful preventative therapies for nicotine addiction, the state of the art requires vast amounts of data from both *in vitro* and *in vivo* experiments,

utilizing *in vivo* animal models, *in vivo* experiments to determine efficacy, toxicity, etc. prior to clinical trials (e.g. Phase 0 studies) without guaranteed success in humans (e.g. Phases I-IV). For example, Kosten et al. (Pharmacology & Therapeutics 108: 76-85, 2005 and Vaccine 20: 1196-1204, 2002) teach various potential disadvantages to hapten-protein conjugate vaccination (i.e. active immunization) including requirement for multiple boosters since exposure to haptens does not induce antibody production (e.g. no secondary response); the carrier must be highly immunogenic in order to produce sufficient antibody levels; several factors can alter antibody serum levels including the quality of the vaccine, dose, frequency of boosters, time interval between boosters, etc.; patient compliance particularly in drug abusers; potential for allergic reactions to proteins conjugated to haptens due to high level of immunogenicity; ability to surmount the effects of vaccination via using higher doses of drug (i.e. prevention difficult); 2-6 months required to produce sufficient antibody titers; etc. (please refer to entire reference, particularly page 78, right column; page 79, right column). In addition, Rose (2008, Ann. N.Y. Acad. Sci., 1141: 233-256) teaches that animal studies have shown antibody concentrations of 440 nM in response to nicotine vaccines (see the entire references particularly page 241). However, this amount of nicotine antibodies would only bind the dose of nicotine in less than five puffs of a typical cigarette. Therefore, the available antibody would quickly become saturated and nicotine inhaled form subsequent inhalation of cigarette smoke would bypass the saturated antibodies. Furthermore, nicotine vaccines might not relieve withdrawal symptoms. Cerny et al. (2008 Expert Opin. Investig. Drugs 17(5): 691-696) teach that of the three nicotine vaccines in clinical trials including *Pseudomonas aeruginosa* exoproetein A conjugated to 3'-aminomethylnicotine (i.e. Nabi Pharm.) require high dosages to obtain sufficient antibody

responses and has a relatively high incidence of side effects (please refer to the entire reference particularly pages 693 and 695). Therefore, the level of predictability in the art is dependent on many factors including the specific formulation of the nicotine-protein conjugate, dosage, multiple boosters provided at distinct intervals, patient compliance, etc. While treating addiction to nicotine is important, the state of the art requires vast amounts of data including Phase 0-IV trials.

The level of skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction provided by the inventor and the existence of working examples:

There are no specific examples directed to the presently claimed invention of a nicotine or nicotine derivative linked to *Pseudomonas* exotoxin which elicits nicotine-specific antibodies in humans; nor is there any guidance as to how to specifically utilize a pharmaceutical composition comprising a nicotine or nicotine derivative linked to *Pseudomonas* exotoxin which elicits nicotine-specific antibodies in humans which is within the scope of the presently claimed invention.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

In light of the unpredictability surrounding the claimed subject matter, the undue breadth of the claimed invention's intended use, and the lack of adequate guidance, one wishing to practice the presently claimed invention would be unable to do so without engaging in undue experimentation. One wishing to practice the presently claimed invention would have to produce additional *in vitro* experiments utilizing animal models for preventing nicotine addiction to

determine if the pharmacological and psychologically addictive effects of nicotine are altered and perform Phase I-IV clinical trials. In addition, *in vitro* and clinical trials for nicotine and every possible nicotine derivative would be necessary (see present claim 125).

20. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

21. Claims 125-126, 128, 131-138, and 142 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, independent claim 125 refers to "nicotine derivative". However, "nicotine derivatives" are not defined by the present specification. Do "nicotine derivatives" include nicotine metabolites (see present Figure 19), nicotine conjugated to the linkers (see present Figures 17B and 18; formulas of various CJ reference numbers)? If "nicotine derivative" refers to nicotine conjugated to the linkers, then the recitation of "nicotine derivatives" and the specific structure of the linker (i.e. various CJ reference numbers in present claim 125) appears to be redundant in the claims. Does a nicotine derivative require a specific core structure? Does a nicotine derivative include any altered form of nicotine (e.g. peptide addition, chemical addition, metabolites, etc.)?

Maintained Rejections

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 125-126, 128, 131-138, and 142 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,876,727 alone or in combination with Green et al. U.S. Patent 5,601,831. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed inventions and the inventions as claimed in U.S. Patent No. 5,876,727 claim nicotine or nicotine-derived haptens conjugated to a carrier and pharmaceutical compositions of the hapten-carrier.

For present claims 125 and 142, U.S. Patent No. 5,876,727 claims a nicotine hapten-carrier conjugate comprising the structure shown in Figures 17b and 18 (e.g. nicotine derivative hapten wherein chemical moieties may be at positions A-F and not simply utilized as a linker between the hapten and the carrier) and side chains (e.g. branch) of CJ 0, 1, 1.1, 1.2, 1.3, 2, 2.1, 2.2, 2.3, 3, 3.1, 4, 4.1, 5, 5.1, 6, 7, 7.1, 8, 8.1, 9, 10, and 11 (where the CJ structures are claimed, n = an integer, and Q is a carrier) and a T-cell epitope carrier (please refer to claim 1). In addition, U.S. Patent 5,876,727 claims carriers including peptides, proteins, cholera toxin,

diptheria toxin, tetanus toxoid, and pertussis toxin (i.e. bacterial toxins; please refer to claim 1). Column 13, lines 45-49 of U.S. Patent 5,876,727 teaches pseudomonas exotoxin carriers. In addition, Green et al. teaches that pseudomonas exotoxin can be utilized as a carrier for hapten vaccines (see the entire specification particularly the abstract; columns 2, 10-12; claim 9).

For present claim 126, U.S. Patent 5,876,727 claims n is from 3 to 20 (please refer to claim 1).

For present claim 128, U.S. Patent 5,876,727 claims at least two haptens coupled to the carrier (e.g. greater than one hapten; please refer to claim 2).

For present claims 131-132, U.S. Patent 5,876,727 claims a pharmaceutically acceptable carrier, an aqueous solution at a physiologically acceptable pH, and adjuvants (e.g. pharmaceutically acceptable excipient; please refer to claims 8-11).

For present claim 133-135, U.S. Patent 5,876,727 claims alum (i.e. aluminum hydroxide), MF59, or RIBI adjuvants (please refer to claims 9-10).

For present claims 136 and 139, U.S. Patent 5,876,727 claims pharmaceutically acceptable carriers, adjuvants, alum, MF59, RIBI, and aqueous solutions (e.g. auxiliary agent or supplementary active compound; please refer to claims 8-11).

For present claim 137, U.S. Patent 5,876,727 claims parenternal administration to a mammal (e.g. human; please refer to claims 12 and 17).

For present claim 138, U.S. Patent 5,876,727 claims oral administration (please refer to claims 12 and 18).

Therefore, the claims of U.S. Patent 5,876,727 render the presently claimed invention *prima facie* obvious.

Arguments and Response

24. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 5,876,727 for claims 125-126, 128, 131-138, and 142 were considered but are not persuasive for the following reasons.

Applicants contend that the rejection relies on Walling et al. (see page 12 of the response received on June 11, 2009).

Applicants' arguments are not convincing since the claimed invention of 5,876,727 renders obvious the pharmaceutical composition of the instant claims and Walling is not relied upon for the rejection. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

25. Claims 125-126, 128, 131-138, and 142 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 88, 90, 103, 106, 108-109, and 128-135 of copending Application No. 11/472,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed inventions and the inventions claimed in U.S. Patent application 11/472,215 claim nicotine hapten-carrier conjugates and pharmaceutical compositions.

For present claims 125, 128, 131, and 142, U.S. application 11/472,215 claim a nicotine hapten or nicotine derivative hapten-carrier conjugate comprising the structure shown in Fig. 17b (e.g. nicotine derivative hapten) and branches of CJ 0, 1, 1.1, 1.2, 1.3, 2, 2.1, 2.2, 2.3, 3, 3.1, 4,

4.1, 5, 5.1, 6, 7, 7.1, 8, 8.1, 9, 10, and 11 wherein Y (e.g. for the CJ structures) is S, O, or NH (where the CJ structures are claimed, n = an integer, and Q is a carrier) and a T-cell epitope carrier (please refer to claims 88 and 91). In addition, U.S. application 11/472,215 defines bacterial toxin carriers as including pseudomonas exotoxin (see the specification).

For present claim 126, U.S. application 11/472,215 claim n is from 3 to 20 (please refer to claim 90).

For present claims 132, U.S. application 11/472,215 claim adjuvants (please refer to claim 103).

For present claim 133, U.S. application 11/472,215 claim alum, MF59, or RIBI adjuvants (please refer to claims 106 and 108).

For present claim 134-135, U.S. application 11/472,215 claim aluminum hydroxide or aluminum phosphate (please refer to claim 108).

For present claim 136, U.S. application 11/472,215 claim pharmaceutically acceptable carriers, adjuvants, alum, MF59, RIBI, and aqueous solutions (e.g. auxiliary agent or supplementary active compound; please refer to claims 103, 106, and 108).

For present claim 137, U.S. application 11/472,215 claim parenteral administration to a mammal (e.g. human; please refer to claims 109 and 128-135).

For present claim 138, U.S. application 11/472,215 claim oral administration (please refer to claims 109 and 128-135).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Arguments and Response

26. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 11/472,215 for claims 125-126, 128, 131-138, and 142 were considered but are not persuasive for the following reasons.

Applicants contend that the rejections should be held in abeyance.

Applicants' arguments are not convincing since the claimed inventions of 11/472,215 renders obvious the pharmaceutical composition of the instant claims. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

27. Claims 125-126, 128, 131-138, and 142 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 119-135 of copending Application No. 11/472,220; claims 88-89, 95, 98-99, 102-103, 106, 108, 110, 115-116, 119-120, 123-124, and 127-128 of 11/472,219; and claims 88, 92, 97, 100, 103, 105, 110, 113, 115, 118, and 122-127 of 11/472,217. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed invention is drawn to a pharmaceutical composition which implies a method of treating/method of eliciting an immune response as claimed in U.S. applications 11/472,217; 11/472,219; and 11/472,220.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Arguments and Response

28. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 11/472,220; 11/472,219; and 11/472,217 for claims 125-126, 128, 131-138, and 142 were considered but are not persuasive for the following reasons.

Applicants contend that the rejections should be held in abeyance.

Applicants' arguments are not convincing since the claimed inventions of 11/472,220; 11/472,219; and 11/472,217 render obvious the pharmaceutical composition of the instant claims. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

July 23, 2009